GPI-80 defines self-renewal ability in hematopoietic stem cells during human development.

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Public Summary:
Advances in generating human stem cells from non-embryonic origins have given us the hope of generating adult blood stem cells in the laboratory for the treatment of blood diseases and disorders, including bone marrow transplants for cancer patients. This study brings us closer to understanding the necessary components needed for culturing these adult blood stem cells in the laboratory.

Scientific Abstract:
Advances in pluripotent stem cell and reprogramming technologies have given us the hope of generating hematopoietic stem cells (HSCs) in culture. To succeed, greater understanding of the self-renewing HSC during human development is required. We discovered that the glycophosphatidylinositol-anchored surface protein GPI-80 defines a subpopulation of human fetal liver hematopoietic stem/progenitor cells (HSPCs) with self-renewal ability. CD34(+)CD38(lo/-)CD90(+)GPI-80(+) HSPCs were the sole population that maintained proliferative potential and an undifferentiated state in stroma coculture and engrafted in immunodeficient mice. GPI-80 expression also enabled tracking of HSPCs once they emerged from endothelium and migrated between human fetal hematopoietic niches. GPI-80 colocalized on the surface of HSPCs with Integrin alpha-M (ITGAM), which in leukocytes cooperates with GPI-80 to support migration. Knockdown of GPI-80 or ITGAM was sufficient to compromise HSPC expansion in culture and engraftment in vivo. These findings indicate that human fetal HSCs employ mechanisms used in leukocyte adhesion and migration to mediate HSC self-renewal.